

Introducing Precision Medicine into an Undergraduate Medical Curriculum: An Interactive Lecture and Case-Based Learning Activity

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Mara Rao, BSE¹; Christin Traba, MD, MPH²; Joshua Kra, MD^{3,4}; Malcolm D. Mattes, MD⁵

¹Rutgers New Jersey Medical School, Newark, New Jersey, USA; ²Department of Pediatrics, Rutgers New Jersey Medical School, Newark, New Jersey, USA; ³Division of Hematology/Oncology, Rutgers Cancer Institute, Newark, New Jersey, USA; ⁴Division of Hematology/Oncology, Department of Medicine, Rutgers New Jersey Medical School, Newark, New Jersey, USA; ⁵Department of Radiation Oncology, Rutgers Cancer Institute, New Brunswick, NJ, USA

Corresponding author: Mara Rao, mwr80@njms.rutgers.edu, ORCID 0009-0008-3912-4349

Online Resource 1: a) Precision medicine educational session learning objectives, b) introductory lecture topics, c) outline of clinical case content, and d) pre- and post-assessment subjective and objective questions with answers to objective questions.

a) Session learning objectives:

- I. Knowledge of precision medicine concepts
 - A. Define precision medicine and recognize differences from traditional medicine
 - B. Identify examples of precision medicine across different specialties
 - C. Gain familiarity with current and emerging precision medicine diagnostic and therapeutic tools
- II. Application of precision medicine concepts
 - A. Identify clinical scenarios in which precision medicine tools can be leveraged to enhance patient care
 - B. Discuss the use of precision medicine tools in an oncology-related clinical case
 - C. Recognize limitations and challenges in precision medicine implementation in a clinical scenario

b) Introductory lecture topics outline:

- I. Definitions
 - A. Definitions of precision medicine
 - B. Comparison of traditional medicine versus precision medicine
 - C. Examples of precision medicine across specialties
 - D. Definitions of related terms:
 - 1. Personalized medicine
 - 2. Stratified medicine
 - 3. P4 medicine
- II. Timeline of precision medicine milestones
 - A. Early targeted therapies
 - 1. Tamoxifen
 - 2. Trastuzumab
 - 3. Imatinib
 - B. Human genome project
 - C. Next generation sequencing
 - D. Patient-derived xenografts and organoids
 - E. Therapeutic cancer vaccines
 - F. CRISPR Cas9
 - G. Immune checkpoint inhibitors
 - H. US precision medicine initiative
 - I. Antibody drug conjugates
 - J. CAR T-cell therapy
 - K. The cancer genome atlas
 - L. Current precision medicine FDA approvals
- III. Limitations and challenges of precision medicine
 - A. Barriers to implementation
 - B. Cost and accessibility
 - C. Cost-effectiveness of targeted therapies
 - D. Exacerbation of health disparities
 - E. Privacy and patient security considerations
- IV. Future directions for precision medicine
 - A. Convergence of artificial intelligence and precision medicine
 - B. Clinical applications of circulating tumor DNA

c) Clinical case topics outline:

- I. Patient presentation: history, physical exam findings
- II. Diagnostic workup: imaging, biopsy, histology, staging
- III. Palliative treatment of cancer symptoms
- IV. Management of non-small cell lung cancer (NSCLC) without targetable driver mutations
- V. Biomarker testing in NSCLC: PD-L1, EGFR, ALK, ROS1, BRAF

- VI. Management of EGFR-mutated NSCLC
 - A. RAS-RAF-MEK-ERK pathway
 - B. Tyrosine kinase inhibitor mechanism of action
 - C. Tyrosine kinase inhibitor mechanisms of resistance
 - D. BRAF and MEK inhibition
- VII. Liquid biopsy
- VIII. Tumor heterogeneity
- IX. Metastasis-directed therapy
- X. Palliative care

d) Pre- and post-assessment questions:

Part 1: Perceived abilities and attitudes related to precision medicine

1. Rate the degree to which you agree that you can accomplish the following: Recognize differences between precision medicine and traditional medicine
 - a. Strongly disagree
 - b. Disagree
 - c. Neutral
 - d. Agree
 - e. Strongly agree
2. Rate the degree to which you agree that you can accomplish the following: Understand diagnostic and therapeutic platforms used in precision medicine
 - a. Strongly disagree
 - b. Disagree
 - c. Neutral
 - d. Agree
 - e. Strongly agree
3. Rate the degree to which you agree that you can accomplish the following: Apply principles of precision medicine in clinical scenarios to improve patient care
 - a. Strongly disagree
 - b. Disagree
 - c. Neutral
 - d. Agree
 - e. Strongly agree
4. Rate the degree to which you agree with the following statement: "The topic of precision medicine is important to learn in order to become an effective physician"
 - a. Strongly disagree
 - b. Disagree
 - c. Neutral
 - d. Agree
 - e. Strongly agree
5. Rate the degree to which you agree with the following statement: "My medical education has adequately prepared me to practice precision medicine"
 - a. Strongly disagree
 - b. Disagree
 - c. Neutral
 - d. Agree
 - e. Strongly agree
6. (Post-assessment only) Rate the degree to which you agree with the following statement: "I plan to apply what I have learned to the practice of medicine in the future"
 - a. Strongly disagree
 - b. Disagree
 - c. Neutral
 - d. Agree
 - e. Strongly agree
7. (Post-assessment only) Please comment on the strengths of this activity.

8. (Post-assessment only) Please comment on how this activity could be improved.

Part 2: Knowledge and application of content from lecture and clinical case

1. Which of the following correctly pairs a precision medicine-related term and its definition?
 - a. Traditional medicine: A systems approach to medicine that includes predictive and participatory aspects
 - b. **Stratified medicine: The grouping of patients based on risk of disease or response to therapy by using diagnostic tests or techniques**
 - c. P4 medicine: A form of medicine that uses information about a person's genes, proteins, environment, and lifestyle to prevent, diagnose, or treat disease
 - d. Personalized medicine: Therapies are matched with specific patient population characteristics using clinical biomarkers
2. Your patient has recently been diagnosed with acute lymphoblastic leukemia, and you are reviewing different treatment options. Which specific biomarker would be required to use imatinib as a targeted therapy for this patient?
 - a. CD19 expression
 - b. TdT expression
 - c. BCL-2 overexpression
 - d. PML-RARA fusion gene
 - e. **BCR-ABL fusion gene**
3. Which of the following is a feature of next generation sequencing (NGS)?
 - a. Higher sensitivity and higher cost than Sanger sequencing
 - b. Sequences fragments up to 1 million base pairs
 - c. **Uses bridge amplification and sequencing by synthesis**
 - d. Uses size separation by capillary gel electrophoresis
4. Which of the following is an advantage of patient-derived xenografts to model disease?
 - a. Lower cost and labor requirements compared to traditional cell culture
 - b. Enables high-throughput screening of different therapeutic agents
 - c. **Captures the genetic features and heterogeneity of a patient's tumor**
 - d. Simulates the patient's immune system
5. A patient with newly diagnosed metastatic colorectal cancer presents to your office for a second opinion regarding treatment options. He has read about immunotherapy online and is interested in immune checkpoint inhibitors. Which of the following features would you assess to best predict his response to pembrolizumab?
 - a. Level of tumor microenvironment heterogeneity
 - b. Tumor-associated macrophage count
 - c. CTLA-4 expression level
 - d. **Mismatch repair deficiency or microsatellite instability phenotype status**
6. Which patient is most likely to benefit from trastuzumab-deruxtecan?
 - a. **A patient with HER2 3+ endometrial cancer**
 - b. A patient with HER2-negative ovarian cancer
 - c. A patient with ER+/PR- breast cancer
 - d. A patient with BRCA2-mutated breast cancer
7. Your patient with non-small cell lung cancer has a mutation leading to constitutive activation of KRAS. Considering the relevant signaling pathway, which of the following would not be an effective targeted therapy?
 - a. RAF inhibitor
 - b. MEK inhibitor
 - c. **EGFR inhibitor**
 - d. All of the above would be effective
8. Your patient is being treated with osimertinib, an EGFR tyrosine kinase inhibitor, for widely metastatic non-small cell lung cancer. He initially showed a partial response, but follow-up imaging after 12 months of treatment shows increased growth of his existing tumors and new metastatic sites. Which of the following is an appropriate next step in management?
 - a. Increase the dose of the TKI and rescan after 3 months
 - b. Switch to a second-generation TKI

- c. **Perform a liquid biopsy**
 - d. Discontinue systemic therapy and refer him to surgery
- 9. Describe two current challenges or limitations related to precision medicine.
 - a. Possible answers include: barriers to adoption and implementation of precision medicine practices; lack of patient accessibility due to cost of precision medicine diagnostic tools and therapies; variable cost-effectiveness of targeted therapies based on improvement in clinical outcomes; exacerbation of health disparities due to lack of representation in genomic studies; and ethical considerations related to patient privacy and information security. Maximum score of 1 point. Partial credit was given (0.5 points) if only one challenge was correctly described. No credit was given for the answer “time” without further explanation.
- 10. Explain when metastasis-directed therapy is used.
 - a. Metastasis-directed therapy (MDT) involves local consolidative treatment of metastatic lesions, such as surgical metastasectomy or stereotactic ablative radiotherapy. MDT can be used for patients with oligometastatic disease, which is defined as having a limited number of metastatic sites (1-5), as opposed to widely metastatic disease. MDT can lead to prolongation of disease control and survival benefits when added to systemic therapy, which is often not curative. Maximum score of 1 point. Partial credit was given (0.5 points) for answers such as palliative care and tumor heterogeneity that did not reference oligometastatic disease.