University of Pittsburgh School of Medicine

Personalized Medicine: The Impact of Molecular Testing on Patient Care Mini-Elective

Spring 2017

Course Dates:	January 27, February 3, 10, 17, 24 Fridays, 2:30-4:30 PM
Maximum Students:	5
Class Year:	MS1 and MS2
Course Directors:	Simion Chiosea, MD Associate Professor of Pathology Somak Roy, MD Assistant Professor of Pathology
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Description:

Personalized medicine applies knowledge of molecular data for early disease detection, targeted treatment, and detection of person's predisposition to a particular disease. It improves diagnosis and treatment of a disease and advances effectiveness of healthcare.

This mini-elective is based in the Department of Pathology and will introduce students to principles and current applications of personalized medicine. During mini-elective students will be able to observe and discuss the principles of molecular testing, become familiar with the clinical interpretation of molecular results in all areas of medicine, including oncology, neuro-oncology, endocrinology, and gastroenterology.

The training will be conducted in the clinical Molecular And Genomic Pathology (MGP) laboratory, Department of Pathology, University of Pittsburgh. MAP laboratory is one of the largest laboratories in the US focused on molecular diagnostics of solid tumors. It processes over 4,000 samples each year using the traditional molecular biology techniques and novel array-based methodologies, including next generation sequencing. It performs molecular testing for all hospitals of the UPMC system and serves as reference laboratory for other medical centers.

The students will be exposed to various molecular tests (1p/19q deletion and MGMT methylation in brain tumors, microsatellite instability [MSI] in colorectal and endometrial cancer, preoperative detection of mutations in thyroid cancer, identification of *EGFR* and *KRAS* mutation in lung and colon cancers, etc.) and learn their implications for clinical practice. They will have opportunity to learn and observe molecular techniques (nucleic acids isolation, PCR, real-time PCR, next generation sequencing, direct

nucleotide sequencing, and gene expression profiling, etc.) and become familiar with basic administrative technical, safety and quality control issues pertinent to the clinical molecular testing.

The course will be based on presentation of individual real-life cases that illustrate the day to day practice in one of the largest molecular laboratories.

Objectives:
- To learn the principles of personalized molecular medicine
- To become familiar with molecular testing available to patients with neoplastic diseases
- To understand the physician's role in ordering of molecular tests.
- To understand the diagnostic utility and clinical implication of molecular test results with respect to patient management, treatment and prognosis.

Requirements:
- Participation in all class sessions.
- Completion of assigned reading from current literature (listed below).

Class format:
During each session, the student will be meeting with the faculty of the Division of Molecular Pathology to review principles of molecular testing in specific area of medicine followed by real-life case sign out. The case sign out will include microscopic evaluation of tumor that is subjected to molecular analysis, review of molecular results (i.e. sequencing, real-time PCR, etc.), and discussion of the results with respect to patient management. Students will look up specific molecular tests as they review cases and will take notes on key molecular features in brain tumors, lung, colon, pancreas, thyroid carcinomas and other neoplastic diseases. Students will finish each afternoon session with reviewing of molecular results for 2- 5 patients. Ample time for direct interaction with faculty will be provided at all times.

Location:
Molecular Anatomic Pathology Sign Out Room; UPMC Clinical Lab Building. 8th Floor, Room 8039, 3477 Euler Way, OR Department of Surgical Pathology, Presbyterian University Hospital, A-613, Multi-headed microscope sign out room, 200 Lothrop St, Pittsburgh, PA 15213

Session 1—January 27th, 2017
Next Generation Sequencing and other molecular testing for personalized patient care. Tour of the Molecular laboratory.

Assigned reading:
None

Session 2—February 3rd, 2017
Molecular testing of brain tumors including detection of IDH1 and 2 mutations/19q chromosomal deletion and its application for diagnosis and prognosis. Detection of the MGMT gene methylation and its role in current algorithm for targeted treatment of glioma patients with Temozolomide (alkylating agent).

Assigned reading:
Hegi et al. *MGMT* Gene Silencing and Benefit from Temozolomide in Glioblastoma. 2005 N Engl J Med 352: 997-1003.
Neuro Oncol. 2016 Mar;18(3):379-87. Targeted next-generation sequencing panel (GlioSeq) provides comprehensive genetic profiling of central nervous system tumors. Nikiforova MN et al.

Session 3—February 10th, 2017
- Molecular testing of thyroid ultrasound guided fine needle aspiration specimen for preoperative detection of various mutation important for diagnosis and surgical management of patients with thyroid and pancreatic neoplasms.

Assigned reading:
Targeted next-generation sequencing panel (ThyroSeq) for detection of mutations in thyroid cancer. Nikiforova MN, Wald AI, Roy S, Durso MB, Nikiforov YE. J Clin Endocrinol Metab. 2013 Nov;98(11):E1852-60.

Session 4—February 17, 2017

Tour of the pathology Grossing Room and pathology archive.

Molecular testing of lung tumors for presence of *EGFR* and *KRAS* mutations and their role in guiding therapy with anti-EGFR tyrosine kinase inhibitors.

Assigned reading:

Molecular Pathology and Personalized Medicine: The Dawn of a New Era in Companion Diagnostics-Practical Considerations about Companion Diagnostics for Non-Small-Cell-Lung-Cancer.
Plönes T, Engel-Riedel W, Stoelben E, Limmroth C, Schildgen O, Schildgen V.
J Pers Med. 2016 Jan 15;6(1).

Session 5—February 24, 2017

- Molecular testing of colorectal cancer including detection of *KRAS, PIK3CA,* and *BRAF* mutations and predictive value of these mutations in treatment of metastatic colorectal cancer patients with Cetuximab (anti-EGFR monoclonal antibody) and chemotherapy.
- Detection of MSI in colorectal and endometrial cancers and Hereditary Nonpolyposis Colorectal Cancer (HNPCC) syndrome surveillance.
- Molecular testing of pancreatic fine needle aspirates

Assigned reading:

Chapter 19. Hereditary Nonpolyposis Colorectal Cancer by E.C. Thorland and S.N Thibodeau, pp. 223 – 231 in Molecular Pathology in Clinical Practice, edited by D.G.B. Leonard.

Precision medicine in colorectal cancer: the molecular profile alters treatment strategies.
Tran NH, Cavalcante LL, Lubner SJ, Mulkerin DL, LoConte NK, Clipson L, Matkowskyj KA, Deming DA.
Ther Adv Med Oncol. 2015 Sep;7(5):252-62

Course Evaluation:

Each student will be asked to complete an evaluation of the course at its conclusion.