Personalized Medicine:
The Impact of Molecular Testing on Patient Care
Mini-Elective
Spring 2015

Course Dates: January 23, 30, February 6, 13, 20
              Fridays, 2:00-4:00 PM

Maximum Students: 5

Class Year: MS1 and MS2

Course Directors: Simion Chiosea, MD
                 Associate Professor of Pathology
                 Marina N. Nikiforova, MD
                 Associate Professor of Pathology

Contact Information: Robyn Roche
                    412-647-7065
                    rocher@upmc.edu

                    Angelique Hudec
                    412-802-6797
                    hudecam@upmc.edu

Registration: Betsy Nero, Office of Medical Education
             betsy@medschool.pitt.edu

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 Anatomic Pathology
(MAP) laboratory, Department of Pathology, University of Pittsburgh. MAP la-
boratory is one of the largest laboratories in the US focused on molecular di-
agnostics of solid tumors. It processes over 4,000 samples each year using the
traditional molecular biology techniques and novel array-based methodolo-
gies, 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 \textit{EGFR} and \textit{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,
agarose and capillary gel electrophoresis, 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 23, 2015**
Next Generation Sequencing and other molecular testing for personalized patient care. Tour of the Molecular laboratory.

**Assigned reading:**
None

**Session 2—January 30, 2015**
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:**

**Session 3—February 6, 2015**
- 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.
- Molecular testing of other head and neck cancers.

**Assigned reading:**
Chapter 20: Principles of Molecular Diagnostics in Thyroid Samples, M. Nikiforova, pp. 363 – 375. in Diagnostic Pathology and Molecular Genetics of the Thyroid, edited by YE. Nikiforov.

**Session 4—February 13, 2015**
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:**

**Session 5—February 20, 2015**
- 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:**

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