Personalized Medicine: The Impact of Molecular Testing on Patient Care
Mini-Elective
Spring 2013

Course Dates: January 4, 18, 25, February 1, 8 Fridays, 2:00-4:00 PM

Maximum Students: 5

Class Year: MS1 and MS2

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

Contact Information: Kim Marie Adams
412-647-7065
adamskm2@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 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 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. 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 in colorectal and endometrial cancer, preoperative detection of mutations in thyroid cancer, identification of EGRF 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, 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 MAP 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 Anatomic 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, 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, Room 752 Scaife Hall, 7th floor (two floors above the medical school admission office)

Session 1—January 4, 2013
- Molecular testing of brain tumors including detection of 1p/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 2—January 18, 2013
- Molecular testing of colorectal cancer including detection of KRAS 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 microsatellite instability in colorectal and endometrial cancers and Hereditary Nonpolyposis Colorectal Cancer (HNPCC) syndrome surveillance.

Assigned reading:

Session 3—January 25, 2013
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 4—February 1, 2013**
- 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 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 5—February 8, 2013**
- “Forensic” molecular testing – Identity testing. In rare clinical situations when specimen and/or slide mislabeling occur and when misidentification of the patient is suspected, identity testing is performed.

**Assigned reading:**

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