2022 GET AMPed!

Updates and Case Studies in Molecular Pathology

November 2, 2022
Sheraton Phoenix Downtown, Phoenix, AZ
Room: Valley of the Sun Ballroom DE

7:30am Registration and Continental Breakfast

8:15am

Welcome and Introductions

Alanna Church, MD, *Boston Children's Hospital, Harvard Medical School*

8:20am

Hot Topic: The Inaugural WHO Classification of Pediatric Cancers

Dolores (Lola) López-Terrada, MD, PhD *Baylor College of Medicine and Texas Children's Hospital*

The histological types, molecular characteristics, and pathogenesis of tumors diagnosed in children are different of those in adults. They often lack the genetic complexity of adult malignancies, frequently resulting from unique genetic driver events, such as chromosomal translocations leading to oncogenic fusions. This session will emphasize the diagnostic and clinical challenges that justified the development of the first WHO Classification of Pediatric Tumors, and will summarize the main diagnostic updates including the rapid transition from a mostly histological to a molecularly-driven classification, accounting for recent discoveries in pediatric tumor genomics.

Learning Objectives

- Describe the diagnostic and clinical challenges that led to the development of the first WHO Classification of Pediatric Tumors
- Discuss and provide examples of the multi-layered approach, incorporating morphology, immunohistochemistry, and molecular diagnostic criteria for pediatric cancers
- Identify the most common neoplasms diagnosed in children and their characteristic molecular diagnostic events

9:05am

From the Operating Room to the Laboratory: Pre-analytic Considerations for Tissues

Ying-Chun Lo, MD, PhD, *Mayo Clinic*

An introductory lecture aimed to provide basic pre-analytic factors for tissue molecular testing. Key considerations of pre-analytical steps will be illustrated and useful tips will be proposed. Interactive discussion will be encouraged throughout the lecture.

Learning Objectives

- Structure the pre-analytical steps of tissue from sampling to molecular laboratory
- Describe essential factors for tissue evaluation
- Improve the successful rate of molecular testing

9:35am Break

9:55am

Testing Modalities to Look at Genome Structure: Copy Number and Gene Fusions

Adam Fisch, MD, PhD, *Massachusetts General Hospital*

This session will be an overview of the main testing modalities for the detection of structural variants in neoplasia, which include primarily rearrangements and copy number changes. The lecture will cover arrays, fluorescence in-situ hybridization (FISH), and next-generation sequencing, as well as some of the clinical implications of these findings.

Learning Objectives

- Recognize the utility of each testing modality in detecting different types of structural variants
- Understand the strengths and limitations of each testing modality presented
- Appreciate the clinical implications of the results of testing for structural variants

10:30am

Testing Modalities to Look at Sequence Variants

Marjorie David, MD, MS, *UT Health San Antonio*

Participants will compare the applications of Sanger Sequencing, real-time PCR and next-generation sequencing in an interactive format that integrates a simple case example. Additionally, the mechanisms of each testing modality will be explored.

Learning Objectives

- Compare the applications of Sanger Sequencing, real-time PCR, and next generation sequencing
- Describe the mechanisms of Sanger Sequencing, real-time PCR, and next generation sequencing

Revised 10/17/2022

11:05am

Introduction to Bioinformatics Pipeline & Data Analysis

Timothy Daniel, MLS(ASCP)CMMBCM,QLSCM, *Palmetto GBA*

This session will start with the generation of FASTQ files. It will then go into how alignment occurs and the creation of variant calling. It will then go into annotation and end with reporting to the patients. It will go over useful tools in this process as well as what those tools do. We will talk about best practices for a clinical bioinformatic pipeline.

Learning Objectives

- To understand the process of samples post sequencing
- Learn dry bench details of analysis
- Learn best practices for maintaining a bioinformatic pipeline

11:40am

Designing Molecular Workflows

Thomas Lee, MD, PhD, *UCLA David Geffen School of Medicine*

This session will review some common considerations and pitfalls in designing and implementing a molecular workflow in the clinical laboratory. Topics will include assessment of clinical needs and volume, validation of new assays, and workflow management in the context of laboratory operations.

Learning Objectives

- Describe practical considerations when designing a molecular workflow
- Integrate assay design with laboratory operations
- Recognize situations where production issues may arise

12:15 pm **Lunch**

1:15pm

Introduction and Overview to Interactive Case Breakout Sessions

Alanna Church, MD, *Boston Children's Hospital, Harvard Medical School*

1:20pm

Concurrent BREAK-OUT Sessions (4 sessions x 30 min each, 10 minute break at 2:20pm)

Case Study 1 – Infectious Diseases

Allen Bateman, PhD, MPH, D(ABMM), *Wisconsin State Laboratory of Hygiene*

Cecilia M. Thompson, MS, PhD, D(ABMM), MLS(ASCP)CM

This session will describe a SARS-CoV-2 molecular testing case, including real-time PCR and whole-genome sequencing. The discussion will include troubleshooting of issues of infectious disease testing during a pandemic, and will touch on high-throughput testing and rapid validations of tests with Emergency Use Authorization.

Learning Objectives

- Upon completion, participant will be able to describe ways to ensure the accuracy of patient results when implementing a molecular assay during a pandemic
- Discuss ways in which high-throughput testing is different from low-throughput testing
- Explain the basics of SARS-CoV-2 whole-genome sequencing and its usefulness for tracking variants and ensuring primer/probe sequences are accurate to maintain test accuracy

Case Study 2 – Solid Tumors

Adam Fisch, MD, PhD, *Massachusetts General Hospital*

Ying-Chun Lo, MD, PhD, *Mayo Clinic*

We will review a clinical case of lung cancer in a patient for whom key treatment decisions and timepoints in her clinical course were longitudinally guided by multiple modalities of molecular testing. Testing strategies discussed include next-generation sequencing assays that target different types of genetic alterations, as well as fluorescence in situ hybridization.

Learning Objectives

- Describe the role of molecular testing in the evaluation of solid tumors and guidance of patient treatment
- Recognize some of the testing platforms currently being used in many molecular labs as the standard of care
- Name the key genetic alterations that can be detected using next-generation sequencing

Case Study 3 – Hematopathology

Amir Behdad, MD, *Northwestern University*
Jennifer Bynum, MD, *Northside Hospital*

Recently, both an update to the WHO and a new International Consensus Classification for hematologic malignancies have been released. Many of the updates require integration of morphologic, clinical, and genomic data for diagnosis. In these case studies, faculty will present a small series of cases focusing on myeloid malignancies which highlight both updates from the 2017 WHO and differences in the two recently released systems which are heavily dependent on molecular findings.

Learning Objectives

- Identify several major molecular updates in the diagnosis of myeloid malignancies
- Identify several major molecular differences in the classification of myeloid malignancies based on the updated WHO vs the new International Consensus Classification
- Identify several diagnoses for which an understanding of the fundamentals of molecular changes is necessary for diagnosis

Case Study 4 - Genetics

Yang Cao, PhD *Washington University in St. Louis*
Jeffrey Kleinberger, MD, PhD *University of Pittsburgh Medical Center*

This interactive session will illustrate a case with disorders of somatic mosaicism. In this session, we will demonstrate the utility of high-depth NGS in the detection of both germline and somatic variants, the technical analysis of NGS data to recognize the variant allelic fraction and phase, as well as variant classification and interpretation.

Learning Objectives

- Understand the utility of high-depth NGS in the detection of somatic variants
- Interpret NGS data and identify germline and somatic variants, including the phase of two adjacent variants and the variant allele fraction based on NGS data
- Apply appropriate criteria to variant classification

3:30pm **Closing Remarks, Questions, and Evaluations**

Alanna Church, MD, *Boston Children's Hospital, Harvard Medical School*