Next Generation Bioinformatics: Beyond Simple Variant Calling

Content Committee:

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CERTIFICATE PROGRAM OUTLINE:

	Title	Speaker(s)	Description	Duration
	Welcome Remarks from Content Director	Sabah Kadri, PhD		5 min
	Pre-test			30 min
Section 1	Complexities in the Analysis and Interpretation of NGS Data for Inherited Disorders	Avni B. Santani, PhD	Over the last decade, next-generation sequencing (NGS) has transformed the field of clinical genetic testing. Interpretation of genetic variants in a constantly evolving technology environment continues to be increasingly complex given the dramatic increase in the size of datasets. This requires clinical laboratories to be increasingly vigilant about the adoption of technology and informatics algorithms used in the application of interpretation. Using case studies as examples, this lecture provides specific challenges related to variant interpretation in the context of NGS derived data. We will discuss potential solutions to address these complexities as well as best practices during development and validation of these techniques.	60 min
	Dealing with Highly Homologous Genes in the Context of Medical Sequencing	Birgit Funke, PhD. FACMG	Next-generation sequencing (NGS) is used to interrogate large sets of genes in a diagnostic setting. Regions of high sequence homology are a major challenge and can lead to false-positive and false-negative diagnostic errors. This presentation will provide a perspective on how to deal with medically important genes that have high sequence homology in a diagnostic setting.	35 min
	Finding the "Indel" in the Haystack	Sabah Kadri, PhD	Detection of Insertion and Deletion (Indel) variants from next generation sequencing (NGS) data is challenging for current technologies and software. The problem is further compounded by laboratory approaches (e.g. the type of sequence chemistry) and the specific variant context (e.g. complex variants and difficult genomic regions). This session will discuss the various challenges and novel bioinformatics strategies to enhance the detection of Indel variants from NGS data.	60 min
	Molecular Informatics at Scale for Genomics-based Personalized Cancer Care	Mark Routbort, MD, PhD	Dr. Routbort describes HGVS nomenclature	10 min
	Post-test 1			15 min
	Section 2 Introduction	Weiwei Zhang, PhD		1 min
Section 2	Pipeline Showcase	Jeremy Segal, MD, PhD and Ahmet Zehir, PhD	Each individual laboratory validates its own combination of software and thresholds for their secondary bioinformatics processes. In this session, we will have participants discuss their approaches to analyze data files from cancer sequencing studies (SEQC2). The obtained results and the analytic methods used to generate the results will be presented by each participating institution, after which, the nuances and differences in the bioinformatics analytic approach and the results will be discussed. This session is expected to be both enjoyable and informative with active discussions.	40 min
	Post-test 2			5 min

	Section 3 Introduction	Weiwei Zhang, PhD		2 min
Section 3	Structural Variant Discovery and Considerations for the Clinical Laboratory	Ahmet Zehir PhD	Dr. Zehir talks about the structural variation in the genome and the ways it relates to disease formation and treatment. He focuses on the different strategies to detect and visualize them using next-generation sequencing technologies for the clinical laboratory with a focus in cancer.	35 min
	Structural Variation Detection in Human Disease	Marcin Imielinski, MD, PhD and Ryan Mills, PhD	Structural variations in the form of DNA rearrangements and aneuploidies are well-known genomic alterations underlying human disease. Despite the ubiquitous nature of genome sequencing in basic research and clinical diagnostics, the mutational processes driving structural variation are yet to be well characterized. In this session, the speakers will describe the strengths of different sequencing technologies and informatics algorithms in identifying different types of genomic structural variation in both cancer and individual genomes.	45 min
	Personalized Genomics: Advancing Continuity in Research to Clinical Care	Vincent Magrini, PhD and Catherine E. Cottrell, PhD	Laboratories are increasingly utilizing complementary sequencing technologies for augmentation of data in difficult to characterize genomic regions. This session aims to examine the utility of generating long read data, including single molecule real-time sequencing and linked reads, to elucidate structural variant composition, detect fusion transcripts, quantify repeat expansions, resolve phasing, and improve mapping in repetitive regions. Optimization of such technologies in a development setting paves the way for translational and clinical applications.	50 min
	Benchmarks for Difficult-to-Sequence Genes and Structural Variants	Justin M. Zook, PhD	Dr. Zook describes the benchmarks for difficult-to-sequence genes and structural variants using Genome in a Bottle.	15 min
	RNA-seq for the Detection of Gene Fusions and Other Alterations in Cancer	Kevin Halling, MD, PhD	Transcriptome sequencing (RNA-seq) of cancer samples for expression profiling and variant and gene fusion detection is a well-established method in scientific research and a powerful and rapidly emerging tool in clinical diagnostics. Various whole-transcriptome and targeted RNA sequencing methods as well as associated informatics algorithms have been developed for RNA-seq; however, standards for RNAseq are still evolving. In this session, the speakers will discuss the utility of RNA-seq for profiling tumor samples, including informatics approaches for splicing analysis, gene fusion detection, expressed variant detection, and gene expression analysis.	30 min
	Post-test 3			20 min
	Closing Remarks	Sabah Kadri, PhD		1 min
	Course Evaluation			10 min
	Claiming CME, CMLE, and AMP Certificate of Completion			