JHS 2017 Workshop on Return of Genetic Results

Glossary

ACMG: American College of Medical Genetics and Genomics. Founded in 1991, the College represents providers of genetic services including clinical, cytogenetic, medical, and molecular geneticists, genetic counselors, and other health care professionals committed to the practice of medical genetics. The current mission of the ACMG is to establish a paradigm of genomic medicine through policy statements and evidence-based practice guidelines; to provide education in an effort to grow the genetics workforce; and, to work with policymakers and payers to support the application of genomics into medical practice.

Allele: An alternative form of a gene or genetic element such as an enhancer. Alleles have been created by mutations and can be responsible for variations in a phenotype.

Chromosome: a structure within a cell made up of DNA and proteins that stores genetic information. There are 23 pairs of chromosomes in the human genome. A chromosome abnormality is an extra and/or missing chromosome or part of a chromosome.

CLIA: Clinical Laboratory Improvement Amendments (CLIA) of 1988 are United States federal regulatory standards on personnel and procedures that apply to all clinical laboratory testing performed on humans in the United States, except clinical trials and basic research. These standards require clinical laboratories to be certificated by their state as well as the Center for Medicare and Medicaid Services (CMS) before they can accept human samples for diagnostic testing. The Centers for Medicare & Medicaid Services (CMS) regulates all laboratory testing (except research) performed on humans in the U.S. through the Clinical Laboratory Improvement Amendments (CLIA).

DNA: Deoxyribonucleic acid is a chemical that carries genetic information and is usually present in a cell as two paired complementary strands. Each strand is a chemical chain made up of four chemical units (abbreviated A, C, T, and G). Genes are carried in the form of a genetic code in a strand.

Gene: A unit of inheritance, normally made up of a region of DNA, that codes for a protein or for an RNA chain. A gene mutation is a change in the region of DNA that makes up a gene. This change can be as small as a single chemical unit (A, C, G, or T) in the DNA.

Genome: The complete set of genetic information in an organism. The genome provides all of the information an organism requires to develop and function. A genome includes protein-encoding genes, genes that do not encode proteins, the regulatory regions of genes, and sequences of DNA whose functions remain to be determined. The study and analysis of genomes is called genomics.

Genotype: An organism's collection of genetic information that determines its physical, chemical, and biological characteristics or traits. "Genotype" is often used more specifically to describe the form of a particular variant that an individual carries.

HIPAA: An acronym that stands for the Health Insurance Portability and Accountability Act, a US law designed to provide privacy standards to protect patients' medical records and other health information provided to health plans, doctors, hospitals and other health care providers.

Penetrance: The proportion of organisms that carry a particular variant of a gene that also expresses the associated trait or phenotype. In medical genetics, penetrance refers to the proportion of individuals carrying a genotype that manifest a related trait or the symptoms of an illness.

Phenotype: The set of individual's biological and physical traits, such as skin color and eye color, as well as complex traits such as blood pressure. "Phenotype" can also be used to describe a specific trait or condition.

Protein: A chemical made up of a chain of amino acids that is created when a gene is translated. There may also be post-translational modifications such as glycosylation (addition of a sugar molecule) or other processing.

RNA: Ribonucleic acid is a chemical that performs several functions in the cells, including acting as an "intermediate" message for a gene to be translated into a protein. RNA is composed of a chain of chemical units (abbreviated as A, C, G, and U) connected along a sugar-phosphate backbone.

TOPMed: Trans-Omics for Precision Medicine. *Trans-Omics for Precision Medicine* (TOPMed), sponsored by the National Institutes of Health's National Heart, Lung and Blood Institute (NHLBI), is a program to generate scientific resources to enhance our understanding of fundamental biological processes that underlie heart, lung, blood and sleep disorders (HLBS). It is part of a broader *Precision Medicine Initiative*, which aims to provide disease treatments that are tailored to an individual's unique genes and environment. TOPMed will contribute to this initiative through the integration of whole-genome sequencing (WGS) and other –omics (e.g., metabolic profiles, protein and RNA expression patterns) data with molecular, behavioral, imaging, environmental, and clinical data. In doing so, this program seeks to uncover factors that increase or decrease the risk of disease, identify subtypes of disease, and help to develop more targeted and personalized treatments.

The *Whole Genome Sequencing* (WGS) project is part of NHLBI's TOPMed program and serves as an initial step for the larger initiative. In recent years, genetic research of complex disease using Genome-Wide Association Study (GWAS) and Exome-sequencing approaches has resulted in an unprecedented explosion of genetic discovery. However, a large portion of heritability in complex diseases remains elusive. Whole Genome Sequencing (WGS) will provide a comprehensive view of the genome, an opportunity to further understand the genetic architecture relevant to heart, lung, blood, and sleep (HLBS) disorders, and an unprecedented resource to the scientific community.

Trait: A physical, chemical, or biological feature of an organism, such as eye color and cholesterol levels. Traits are determined by genes, and complex traits may be modified by the environment.

Transcription (of genes): The process by which information in DNA is copied into RNA.

Translation (of genes): The process by which genetic information is converted from an RNA message into a protein.