Title: Genetics and Disease

Abstract: Many human diseases are associated with mutations or variations in genetic sequences. Some of these genetic variants are heritable, passed down from generation to generation, while others arise sporadically during an organism’s life and cause diseases such as cancer. Researchers are trying to identify and characterize these genetic alterations in the hopes of improving diagnosis and therapeutic options for patients.

In this video, we will examine the history of genetic disease research, and explore key questions asked by medical geneticists. Various tools used to identify the genetic basis of diseases are then discussed, including genotyping techniques and genome-wide association studies (GWAS). Finally, several current examples of medical genetics research are presented.

Application videos:

1. A Strategy to Identify de Novo Mutations in Common Disorders such as Autism and Schizophrenia **(2534 Thumbnail @ 4:09 – Sequence chromatograms showing de novo mutation)**

Description: In this article, researchers present the study design and sequencing strategies to assess how uninherited, *de novo* mutations might contribute to complex diseases. The steps and criteria for choosing candidate diseases and patient cases, as well as for identifying *de novo* mutations from the sequencing data, are discussed.

2. Detection of Rare Genomic Variants from Pooled Sequencing Using SPLINTER**(3943 Thumbnail @ 0:22 Next-generation sequencing schematic)**

Description: GWAS, which compares the genotypes of affected versus control populations, has been a dominant method for identifying disease-associated genetic variants. Researchers in this video demonstrates an alternate approach, known as pooled sequencing, in which DNA samples from hundreds of patients are pooled, along with both positive and negative control sequences, and subjected to next-generation sequencing. The results are then aligned to the reference genome and analyzed using a custom algorithm called SPLINTER to predict rare, disease-associated variants.

3. Detecting Somatic Genetic Alterations in Tumor Specimens by Exon Capture and Massively Parallel Sequencing **(50710 Thumbnail @ 0:56 – Sequencing data visual from schematic)**

Description: The increasing availability of high-throughput sequencing has made it an appealing option for clinical diagnosis. Here, scientists obtained DNA from paired normal-tumor tissue samples from a group of patients, then specifically captured the protein-encoding exon sequences of 279 cancer-associated genes. The selected DNA was then sequenced to identify potential disease-causing genomic alterations.

4. Infinium Assay for Large-scale SNP Genotyping Applications **(50683 Thumbnail @ 6:00 – Infinium Assay chip)**

Description: This article details the steps to perform a large-scale experiment for genotyping single-nucleotide polymorphisms, where the DNA of dozens or more individuals are hybridized to chips to identify genetic variation at hundreds of thousands of loci simultaneously. This data can then be used in GWAS to determine if any of the genetic variants are disease-associated.

5. Identification of Sleeping Beauty Transposon Insertions in Solid Tumors using Linker-mediated PCR **(50156 Thumbnail @ 0:38 – Schematic of oncogenic genomic sites)**

Description: In this video, researchers demonstrate a genetic screen in mice to identify candidate cancer-associated genes by using random mutagenesis with the *Sleeping Beauty* transposon. After DNA isolation from the resulting tumors, sequences surrounding the transposon insertion sites were specifically amplified and sequenced to find genes that might drive tumor development when mutated.

Related Videos

5042 – Regulating Temperature in the Lab: Preserving Samples Using Cold

5056 – PCR: The Polymerase Chain Reaction

5428 – An Introduction to Modeling Behavioral Disorders and Stress

5545 – Cytogenetics