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CLINICAL EXOME SEQUENCING

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What is an exome?

- Exome consists of all the exons which codes for protein
- About 1-2 % of DNA consists of exons
- Mutations in the exons causes diseases

What is Clinical Exome Sequencing?

- Clinical Exome Sequencing is a test for identifying disease-causing DNA variants within the genome which codes for proteins (exons) or flanks the regions which code for proteins
- It is widely accepted that about 85% of known disease-causing variants occur within the 1% of the genome containing the exons and splice junctions; thus, surveying just this portion of the genome is an efficient and powerful clinical diagnostic tool for individual patients

Why Greenarray- Clinical Exome Sequencing Test?

- Delivers the most accurate and comprehensive exome coverage
- Validation of the sequencing results by sangers sequencing
- Advanced informatics tools improves overall accuracy and sensitivity for calling single nucleotide variants
- High quality exome sequencing, highly sensitive and specific detection of mutations

Advantages of Clinical Exome Sequencing

- Identifies variants across wide range of applications
- Provide cost effective alternative to whole genome sequencing
- Comprehensive coverage of all coding regions
- Smaller and more manageable data for easy analysis

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What all possible genetic diseases are detected in Clinical Exome Sequencing?

- Nutritional and Metabolic Diseases
- Congenital, Hereditary, and Neonatal Diseases
- Cardiovascular Diseases
- Musculoskeletal Diseases
- Respiratory Tract Diseases
- Nervous System Diseases

Who should undergo CES?

- Patients with clinical or genetic heterogeneity
- With clearly genetic disease, but previous genetic testing having been negative
- With an atypical presentation of a genetic disorder
- With a long list of differential diagnoses

One time blood sampling of about 3ml is all required for test!

Is biological parent sample important?

- Biological parents of proband provides relevant information for analyzing the affected individual's exome

- Comparing the probands' exome to their parents' exomic data could show that a pathogenic variant was not inherited from a parent and was new in the proband

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How does sequencing work?

- Greenarray's CES reads the sequence of exome using Next Generation Sequencing
- We isolates the DNA and compares the sequence of the affected individual's exome with the sequence of the exome from healthy people
- This helps to identify any variant that may be cause of medical condition
- Relevant variants detected are then confirmed by Sanger Sequencing

Is Genetic Counseling necessary?

It is recommended to have genetic counseling before and after genetic testing to learn the benefits and limitations of the test.

Necessity of Patient Consent form

- The testing can sometimes detect any additional findings related to one's health
- It may also provide genetic information about family members of the individual being tested
- It is thus necessary to get complete consent of the patient before undergoing a genetic testing

Application of CES

- Rare variant mapping of complex disorders
- Discovery of rare Mendelian Disorders

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How are clinical results reported?

- Not all variants causes genetic disorders
- A clinical exome puts hundreds of sequences together to understand the identified variant and its clinical significance

Variant type	Explanation
Pathogenic Variant	Mutation known to cause the disease
Likely pathogenic Variant	Alterations with strong evidence in favor of pathogenicity
Variant of Unknown Significance	Variant detected is not sure that it is actually causing the genetic disease
No variant detected	No mutation to the reported clinical feature is detected
Additional Findings	A pathogenic variant outside the analysis requested was found

Limitation of CES

- Cannot detect mosaic mutations
- mutations in repetitive or high GC rich regions
- Cannot detect large rearrangements

References

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About Greenarray

Green Array is a molecular diagnostic company. We offers diagnosis of infectious diseases, genetic testing and healthcare information to improve health and wellness. Our goal is to provide high quality affordable and accessible services.

Contact No.: 9823049121