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WHOLE EXOME SEQUENCING GUIDE

What is whole exome sequencing (WES)?

Whole exome sequencing (WES) is a test that analyzes most of our approximately 20,000 genes and is designed to identify genetic changes (variants) in the DNA that may cause disease or are important to the patient's health in other ways. Through WES, thousands of DNA variants are detected. Some variants are disease-causing while others are harmless or have an uncertain effect. This process involves analyzing genes that have been previously associated with human disease, known as characterized genes. Additionally, many human genes have *not* been associated with an underlying genetic condition; these are known as novel genes.

Most changes that cause disease affect the portions of our genes called exons. The exons of a gene contain the genetic information the body uses to make proteins, which are molecules that carry out all the essential functions in the body. The DNA within the exons of all the genes is collectively called the exome. WES is a test that looks for disease-causing changes in any gene that may be related to the patient's underlying clinical presentation.

When should whole exome sequencing (WES) be ordered?

Due to the large and ever-growing number of genes associated with neurodevelopmental disorders, and recent changes in evidence-based recommendations for genetic testing, ordering WES should be considered for patients with neurodevelopmental phenotypes that are not clearly suggestive of a specific disorder or set of disorders. Ordering WES ensures that all potentially clinically relevant genes are considered in the analysis, and can be ordered with family members to clarify inheritance as part of the analysis or as a singleton assay if parental samples are not available. This follows evidence-based clinical guidelines of the American College of Medical Genetics and Genomics (Manickam et al., 2021. Genet Med. 2021 Nov;23(11):2029-2037. PMID: 34211152.)

Who should be included in whole exome sequencing (WES)?

Samples from family members may be studied to help interpret WES results. If biological parents are available to participate in WES, it is recommended to submit their samples as parental samples are the most informative and improves the ability to classify variants. In some cases, when biological parents are not available for testing, including siblings or other biological relatives of the patient can be helpful. In certain situations, such as Rapid Infant WES, limiting testing to the patient may be preferable to allow for a timely analysis. If you are unsure who to include in WES, please contact our office at 406-444-7532 to discuss further.

What is the consenting process?

Informed consent is required for the patient and each family member participating in whole exome sequencing prior to initiating testing. Please refer to our website or contact us at 406-444-7532 to obtain copies of the Patient Whole Exome Sequencing Consent Form and the Family Member Whole Exome Sequencing Consent Form if the ordering provider would like to complete the WES consenting process. Alternatively, Shodair Genetics would be happy to provide consenting services to the patient and each participating family member. The ordering provider may indicate on page two of the WES Test Request Form if they would like assistance with the consenting process.

Who will notify the patient of their whole exome sequencing (WES) results?

The ordering provider is responsible for notifying patients and participating family members of the whole exome sequencing results, as well as the ACMG secondary findings results when applicable. If the ordering provider would like assistance with the interpretation of these results, they may contact our clinical genetics team at 406-444-7564. After the patient and participating family members have been notified of the results, you may send a referral to Shodair Genetics for a genetic consultation to further discuss these results. Referrals should be faxed to 406-444-1064.

Completing the Whole Exome Sequencing Test Request Form

The following sections of the Whole Exome Sequencing Test Request Form are required to be completed. (1) If biological parents or other family members are available to participate in WES, provide each family member's name, date of birth, relationship to the patient, and whether they are affected in the Additional Family Samples section on page one. (2) Prior authorization is required for this testing. Indicate on page one whether prior authorization has been completed or if you would like assistance with prior authorization. (3) Select the appropriate test on page two based on the following: a) If two biological parents or other family members are available to participate in WES, select Trio Whole Exome Sequencing. b) If one biological parent or other family member is available to participate in WES, select Duo Whole Exome Sequencing. c) If there are no biological parents or family members available to participate in WES, select Singleton Whole Exome Sequencing. d) Rapid Infant WES in the NICU setting is limited to testing the patient. Please contact our office at 406-444-7532 to discuss this testing further. (4) Informed consent is required for the patient and each family member participating in WES prior to initiating testing. Indicate on page two whether you have completed the consenting process or if you would like assistance with the consenting process. If you would like assistance with the consenting process, please provide each participating family member's name, date of birth, relationship to patient, phone number, and best time to contact on page two. (5) Please complete the clinical indications on page three.