Medical College of Wisconsin | Genomic Sciences & Precision Medicine Center

Whole Exome / Genome Sequencing Data Analysis (WESDAT / WGSDAT)

Turn Around Time:	**30 Days**
CPT Codes:	**WESDAT – 81417, WGSDAT – 81427**
Test Includes:	✓ **Variant annotation and sequence gap determination using custom software packages** ✓ **Variant Confirmation via Sanger sequencing (if requested)** ✓ **Interpreted Clinical Report**

Expedited WES testing is available. Contact the lab for more information.

Test Description

Whole Genome Sequencing Data Analysis (WGSDAT) / Whole Exome Sequencing Data Analysis (WESDAT) is used to annotate and interpret variants in a patient's genome in order to determine the role of the genomic variants in disease outcomes and to determine the regions of the genome where there is no sequence coverage.

Sample Requirements

Prior arrangements must be made with the laboratory before submission of test request.

Data must be sent on an encrypted media source with the encryption method and password (send separately). Only one patient's data per media source is permitted. Electronic data files can only be accepted for analysis with prior arrangement with lab. Data source will be returned upon request.

If Sanger confirmation of variants is requested:

Whole Blood: 2-4mL of whole blood in a purple top EDTA (2 tubes per patient is preferred). For infants, a minimum of 1mL of blood is required. The tube(s) must be labeled with at least two patient identifiers (patient name/submitter ID number and date of birth). Ship blood tubes overnight at room temperature in an insulated container within 5 days of collection.

gDNA: 5µg of purified gDNA with a minimum of 75ng/µL and a 260/280 purity ratio of 1.75-2.0 in a screw cap tube. The tube must be labeled with at least two patient identifiers (patient name/submitter ID number and date of birth). Ship gDNA overnight at room temperature. Products of genome amplification or other amplification reactions are not accepted.

Test Methodology

Sequence variants are loaded into a commercial software package that contains data sources and algorithms allowing for the evaluation of whole exome / genome sequencing variants for evolutionary conservation, predicted impact on protein structure and function (including Polyphen2 (5) and SIFT (6)), ability to disrupt conserved splice sites, and presence in databases including OMIM, dbSNP, and HGMD (1,2,3). The software annotates variants with this data, taking into account both the reference gene model and any identified alternate transcripts (4). A second commercial software package is used to determine what parts of the genome are not sequenced. If Sanger confirmation of variants is requested, the DNA sequence of a segment of the genome surrounding each variant of interest is PCR amplified from purified genomic DNA followed by sequencing in the forward and reverse directions using automated fluorescent dideoxy sequencing.

Limitations

WESDAT / WGSDAT is validated to evaluate small (generally less than 100 nucleotides in length) substitutions, insertions, and deletions. The ability to detect abnormal variants is dependent on the presence of these variants in the data provided to the laboratory. Certain types of sequence variation are difficult to identify and have not been validated to be reliably detected for current clinical use. These include larger structural variants (SVs) including larger insertions, deletions, copy number variations, triplet repeat expansions, and structural chromosomal rearrangements.

Contact & Submission

GSPMCBusinessOffice@mcw.edu | 414-955-2550

Whole Exome / Genome Sequencing Data Analysis | References

1. Online Mendelian Inheritance in Man, OMIM (TM). Johns Hopkins University, Baltimore, MD. World Wide Web URL: http:// www.ncbi.nlm.nih.gov/omim/ 2. Database of Single Nucleotide Polymorphisms (dbSNP). Bethesda (MD): National Center for Biotechnology Information, National Library of Medicine. World Wide Web URL: http://www.ncbi.nlm.nih.gov/SNP/ 3. The Human Gene Mutation Database: 2008 update. Stenson PD, Mort M, Ball EV, Howells K, Phillips AD, Thomas NS, Cooper DN. Genome Med. 2009 Jan 22;1(1):13. World Wide Web URL: http://www.hgmd.org/ 4. The NCBI handbook [Internet]. Bethesda (MD): National Library of Medicine (US), National Center for Biotechnology Information; 2002 Oct. Chapter 18, The Reference Sequence (RefSeq) Project. World Wide Web URL: http://www.ncbi.nlm.nih.gov/RefSeq/ 5. Ramensky V, Bork P, Sunyaev S. Human non-synonymous SNPs: server and survey. Nucleic Acids Res 30(17):3894-3900 (2002). 6. Kumar P, Henikoff S, Ng PC. Predicting the effects of coding non-synonymous variants on protein function using the SIFT algorithm. Nat Protoc. 2009;4(7):1073-81.