Cordis DX Focus

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Scientific Director: George Nasioulas PhD

SAMPLE INFORMATION

Name :	-	**Date Received :**	-
Medical ID :	-	**Date of Report :**	-
Date of Birth :	-	**Req. Physician :**	-
Location :	-	**Barcode :**	-
Material :	-	**Reason of referal:**	-

Cordis Panel by Next Generation Sequencing: Dyslipidemia

Result

NEGATIVE

NO PATHOGENIC/LIKELY PATHOGENIC VARIANT WAS DETECTED

Methodology

Genomic DNA was extracted from the sample under investigation and was analysed by a solution based capture approach using the target enrichment panel (KapaHyperCap Heredity Panel,ROCHE). Sequencing was carried out using the DNBSEQ-G400 sequencing platform (MGI). Reads were aligned to the reference sequence (GRCh37), and sequence changes were identified and interpreted in the context of a single clinically relevant transcript. Unless otherwise stated, this assay targets all coding regions of the indicated transcripts and 10 base pairs of flanking intronic sequences. The mean coverage was 198X with 99% of all targeted regions sequenced with >=10x depth.

Based on the available patient information, the following diagnostic algorithm was used.

- All genes associated with dyslipidemia and described in the OMIM and HGMD databases were selected.
- Variant classification was performed according to the ACMG AND AMP guidelines (PMID: 25741868)
- Analysis of the mutations with damaging effect (frameshift, nonsense, missense, splicing mutations etc.) as well as de novo mutations was obtained.
- All clinically significant observations were confirmed by Sanger Sequencing analysis on SeqStudio Genetic Analyzer (Thermo Fisher Scientific). The presence of large genomic rearrangements (LGRs), was investigated using the commercial computational algorithm SeqPilotVersion 4.4 Build 505 (JSI Medical System). The presence of LGRs is verified by use the MLPA method (Multiplex Ligation-dependent Probe Amplification, MRC Holland; PMID: 10978226).

*Note:

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Every molecular test has an internal 0,5-1% chance of failure. This is due to rare molecular events and factors related to the preparation and analysis of the samples. Unless otherwise stated, this assay targets all coding regions of the indicated transcripts and 10 base pairs of flanking intronic sequences. Therefore, this method cannot detect variants in deep intronic or enhancer/promoter regions.

The method used achieves 99% sensitivity and specificity for single nucleotide variants and insertions and deletions

Details about non-pathogenic variants

All individuals carry DNA changes (i.e., variants), and most variants do not increase an individual's risk of the disease. When identified, variants of uncertain significance (VUS) are reported. Findings of variants of uncertain significance (VUS) in autosomal recessive diseases are not reported unless they co-exist with another finding (pathogenic, likely pathogenic or VUS in the same gene). Benign variants (Polymorphisms) are not reported and available data indicate that these variants most likely do not cause increased risk of the disease. Present evidence does not suggest that non-clinically significant variant findings be used to modify patient medical management beyond what is indicated by the personal and family history and any other clinically significant findings.

Genes analyzed (Table 1)

APOB	*LDLR*	*LDLRAP1*	*LIPA*	*PCSK9*	*ANGPTL3*	*MTTP*	*SAR1B*	*ABCG5*
AGTR1	*HSD11B2*	*APOE*	*NOS2*	*APOA5*	*APOC3*	*LPL*	*CETP*	*SCARB1*
NPC1	*NPC2*	*FTO*	*MC4R*	*SMPD1*	*SCNN1A*	*SCNN1B*	*SCNN1G*	*LPA*
ABCG8	*LIPC*	*INSIG2*	*SCNN1D*	*STAP1*	*CH25H*	*PLTP*		

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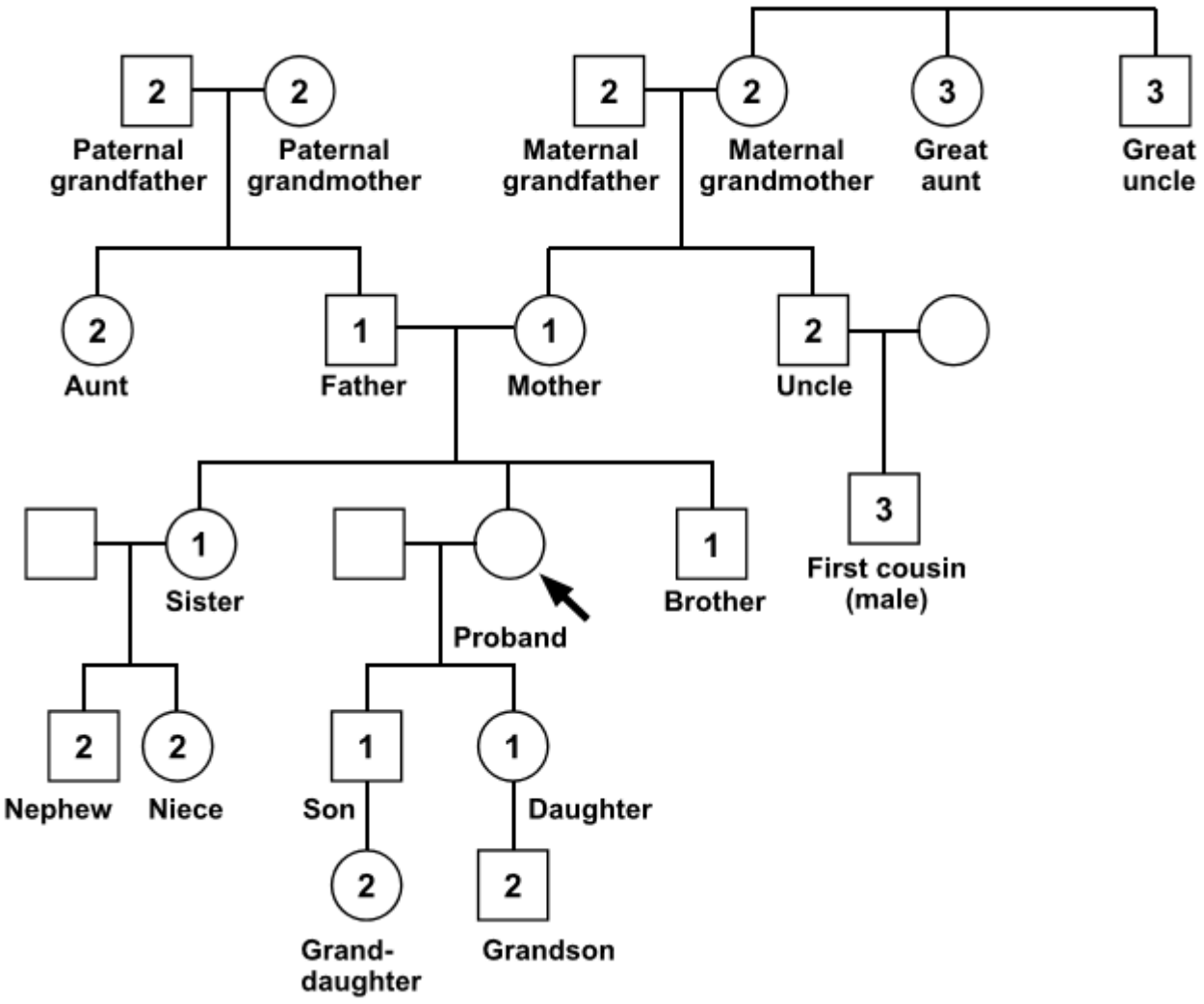
Family tree



Note: The information shown on the family tree has been provided by the patient and not by medical records.

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Literature

1. Richards S, Aziz N, Bale S, Bick D, Das S, Gastier-Foster J, Grody WW, Hegde M, Lyon E, Spector E, Voelkerding K, Rehm HL; ACMG Laboratory Quality Assurance Committee. **Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology.** Genet Med. 2015 May;17(5):405-24. doi: 10.1038/gim.2015.30. Epub 2015 Mar 5. (PMID: 25741868) PMCID: PMC4544753.
2. Harrison SM, Biesecker LG, Rehm HL. **Overview of Specifications to the ACMG/AMP Variant Interpretation Guidelines.** Curr Protoc Hum Genet. 2019 Sep;103(1):e93. doi: 10.1002/cphg.93. (PMID: 31479589) PMCID: PMC6885382.
3. Kalia SS, Adelman K, Bale SJ, Chung WK, Eng C, Evans JP, Herman GE, Hufnagel SB, Klein TE, Korf BR, McKelvey KD, Ormond KE, Richards CS, Vlangos CN, Watson M, Martin CL, Miller DT. **Recommendations for reporting of secondary findings in clinical exome and genome sequencing, 2016 update (ACMG SF v2.0): a policy statement of the American College of Medical Genetics and Genomics.** Genet Med. 2017 Feb;19(2):249-255. doi: 10.1038/gim.2016.190. Epub 2016 Nov 17. Erratum in: Genet Med. 2017 Apr;19(4):484. PMID: 27854360.
4. Landrum MJ, Chitipiralla S, Brown GR, Chen C, Gu B, Hart J, Hoffman D, Jang W, Kaur K, Liu C, Lyoshin V, Maddipatla Z, Maiti R, Mitchell J, O Leary N, Riley GR, Shi W, Zhou G, Schneider V, Maglott D, Holmes JB, Kattman BL. **ClinVar: improvements to accessing data.** Nucleic Acids Res. 2020 Jan 8;48(D1):D835-D844. doi: 10.1093/nar/gkz972. (PMID: 31777943) PMCID: PMC6943040.
5. Köhler S, Gargano M, Matentzoglu N, Carmody LC, Lewis-Smith D, Vasilevsky NA, Danis D, Balagura G, Baynam G, Brower AM, Callahan TJ, Chute CG, Est JL, Galer PD, Ganesan S, Griese M, Haimel M, Pazmandi J, Hanauer M, Harris NL, Hartnett MJ, Hastreiter M, Hauck F, He Y, Jeske T, Kearney H, Kindle G, Klein C, Knoflach K, Krause R, Lagorce D, McMurry JA, Miller JA, Munoz-Torres MC, Peters RL, Rapp CK, Rath AM, Rind SA, Rosenberg AZ, Segal MM, Seidel MG, Smedley D, Talmy T, Thomas Y, Wiafe SA, Xian J, Yüksel Z, Helbig I, Mungall CJ, Haendel MA, Robinson PN. **The Human Phenotype Ontology in 2021.** Nucleic Acids Res. 2021 Jan 8;49(D1):D1207-D1217. doi: 10.1093/nar/gkaa1043. (PMID: 33264411) PMCID: PMC7778952.
6. Rivera-Muñoz EA, Milko LV, Harrison SM, Azzariti DR, Kurtz CL, Lee K, Mester JL, Weaver MA, Currey E, Craigen W, Eng C, Funke B, Hegde M, Hershberger RE, Mao R, Steiner RD, Vincent LM, Martin CL, Plon SE, Ramos E, Rehm HL, Watson M, Berg JS. **ClinGen Variant Curation Expert Panel experiences and standardized processes for disease and gene-level specification of the ACMG/AMP guidelines for sequence variant interpretation.** Hum Mutat. 2018 Nov;39(11):1614-1622. doi: 10.1002/humu.23645. (PMID: 30311389) PMCID: PMC6225902.