Datasheet

Cell3 Target: Exome CG

ExomeCG and Congenica clinicial decision support platform

Highlights

Streamline your workflow

ExomeCG lets you detect all variants (SNVs, indels and CNVs) in a single, clinical-grade assay, suitable for constitutional postnatal and prenatal analysis. Less handling. Less time. More results first time.

Clinically relevant genes

The best coverage of clinical targets thanks to superior CNV detection at loci known to have both gene and exon-level rearrangements. Giving you the option to replace your array and MLPA-based CNV analysis.

Save time. Save resources.

Use as little at 10 ng of DNA unlocking prenatal or limited samples and get results days earlier. ExomeCG saves you time and sample, without compromising on quality or robustness.

Software to support you

ExomeCG fully integrates with the Congenica® clinical decision support platform for data visualisation and analysis. Combined with the Cell3™ Target range, we have your research needs covered, from start to finish.

Introduction

ExomeCG is a clinically enhanced human exome capture kit enabling laboratories to detect all variants (SNVs, Indels and CNVs) in a single, clinical-grade test, suitable for constitutional postnatal and prenatal analysis.

Current clinical cytogenomics workflows consist of multiple tests including Chromosomal Microarrays (CMA), Multiplex Ligation Probe Amplification (MLPA), FISH and NGS (Exome Sequencing). Undertaking multiple tests with different technologies increases associated test cost, time to result and has negative implications for sample input amount required and the cost to process a given sample.

The design of the ExomeCG is formulated to give superior CNV detection at loci known to have both gene and exon level rearrangements, allowing unparalleled coverage of clinical targets and providing an Exome alternative to CMA and MLPA based CNV analysis.

Optimized for use with the Congenica® clinical decision support platform, ExomeCG is a complete solution for calling and analysis of SNVs, indels and CNVs in a single test.

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Expert design

Targeting 51.5 Mb, ExomeCG builds on the Cell3™ Target Whole Exome, with probe enhancement for clinically relevant genes currently targeted with copy number assays such as MLPA, enabling SNV Calling and CNV-detection in one combined test.

Key features

The kit contains all reagents for both library preparation and capture and covers all the standard applications of whole exome sequencing including;

- SNV/Indel detection
- Coverage of all coding exons
- Increased coverage of coding exons of clinically relevant genes
- Inclusion of splice-region sequences
- A CCDS exome design

Key benefits and outcomes

- A single assay for MLPA and CMA sized rearrangements Increased sensitivity
- Cost and workflow efficiencies
- Faster turnaround times
- A fully integrated DNA to report solution – with Congenica platform
- Increased opportunity for diagnosis and reduced time to diagnosis

Product enhancement and outputs

- Enhanced baits around ACMG59 genes
- Extended to include exon level deletions and duplications currently targeted by commercially available kits, such as MLPA, enabling SNV calling and CNV-detection in a single test
- Enhanced for current clinically relevant genes (i.e. OMIM morbid set of 4090 genes)
- Further enhanced with genes associated with prenatal phenotypes (fetal anomalies)
- Further enhanced with transcripts and extra exons for epilepsy (EIEE) genes
- Inclusion of promoter, 5′ and 3′ UTR sequences for current OMIM morbid genes
- Inclusion of non-coding, disease-causing variants (Smedley et al. 2016; Landrum et al. 2018)
- Pharmacogenomic (PGx) markers and sample tracking variants
- Enhanced coverage and bait design around all the design allows for reliable CNV calling in conjunction with Congenica CNV calling pipeline. In particular, the number of bait probes within target regions is increased to better support the statistical model applied by the ExomeDepth CNV caller (Plagnol, 2012)
- Assay can detect CNVs with sizes spanning from single exons up to runs of multiple contiguous genes (~100 bp–40 Mb)
- Designed for use with Reference Genome GRCh38 but can also be used with GRCh37

In-depth features

- Complementing routine rare diseases diagnostics there are additional RefSeq transcripts across OMIM Morbid genes
- Support for prenatal diagnosis using additional transcripts across known fetal anomaly genes
- Havana transcript features associated with known Early Infantile Epileptic Encephalopathy (EIEE) genes for enhanced epilepsy diagnosis
- Excellent coverage of the ACMG59 secondary findings genes (Kalia et al. 2017)
- Previously reported non-coding, disease-causing variants (Smedley et al. 2016; Landrum et al. 2018)
- PGx markers

Ease of use

ExomeCG utilises the Nonacus Cell3™ Target assay; requiring as little as 10 ng of DNA and with a choice of enzyme or non-enzyme fragmentation, the quick and easy workflow can take less than 10 hours, with under 2 hours hands-on time. Manual or automated preparation of between 1 – 96 samples can be performed in a single batch. Up to 384 sample indexes facilitate high throughput laboratories.

Performance

Copy Number Variants

The assay is capable of detecting CNVs with sizes spanning from just a few exons up to multiple contiguous genes (~100 bp–40 Mb); detection of clinically relevant events is achieved with superior precision and recall (Tables 1a and 1b).

Table 1a. Detection of MLPA-confirmed CNVs by the ExomeCG assay. The Bayes factor is the $\log_{10}$ of the likelihood ratio, which quantifies the evidence for the CNV call divided by that for normal copy number.

Affected gene	CNV region	CNV size (bp)	CNV exons	CNV type	Bayes factor
FBN1	exons 29–65	74632	37	deletion	320.0
BRCA1	exons 1–23	77841	24	deletion	190.0
FBN1	exons 1–17	142063	18	deletion	300.0
BRCA1	exons 1–17	57876	18	deletion	200.0
BRCA1	exons 8–13	17956	6	deletion	40.4
BRCA1	exons 8-13	17956	6	deletion	82.4
BRCA2	exons 5–7	513	3	deletion	22.1
NSD1	exons 7–9	6034	3	deletion	34.5
FBN1	exons 60–62	3934	3	deletion	32.8
NSD1	exons 1–3	58095	3	deletion	54.8
BRCA2	exons 1–2	1054	2	deletion	28.3
BRCA1	exons 7–8	311	2	deletion	4.7
BRCA1	exons 8–9	1444	2	deletion	7.5
BRCA1	exon 16	211	1	deletion	14.5
BRCA1	exon 20	84	1	deletion	9.4

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