OneSeq 1Mb CNV Backbone + Custom Panel

Datasheet

Highlights

- Confidently call CNVs, LOH, SNVs and indels in one cost-effective NGS assay
- Streamline your assay and accelerate sample to answer
- Targeting only 2.7 Mb, OneSeq 1Mb CNV backbone can be sequenced on benchtop or high-throughput sequencer

Introduction

Agilent's SureSelect Target Enrichment technology coupled with next generation sequencing (NGS) has been indispensable in uncovering disease-associated mutations such as single nucleotide variations (SNVs) and small insertions & deletions (indels). On the other hand, microarrays remain the primary method to robustly detect copy number variations (CNVs). Based on SureSelect's powerful technology, OneSeq target enrichment is a cost-effective solution to confidently detect all variants in one NGS assay.

The OneSeq 1Mb CNV Backbone + Custom product consists of baits designed to detect CNVs and Loss of Heterozygosity (LOH) genome-wide down to 1Mb and 10Mb resolution, respectively. In addition, OneSeq includes user-defined baits for any Agilent exome, gene or custom panel or custom regions for SNV and indel calling.

OneSeq 1Mb CNV backbone produces highly uniform read depth

Computational methods that identify CNVs from target enrichment data such as whole exome sequencing (WES) are primarily based on the analysis of read depth. These methods make the assumption that read depth from targeted regions is proportional to the number of copies of that region. However, differences in efficiencies of target enrichment baits and sequencing biases produce uneven read depth profiles (Figure 1a) that are not always reflective of copy number changes making CNV calling from WES challenging (Tan *et al.*, 2014). The OneSeq 1Mb CNV backbone has been designed to target genomic regions with optimal GC content and mappability. These features produce highly uniform read depth distribution ultimately resulting in reliable CNV calls genome-wide (Figure 1b).

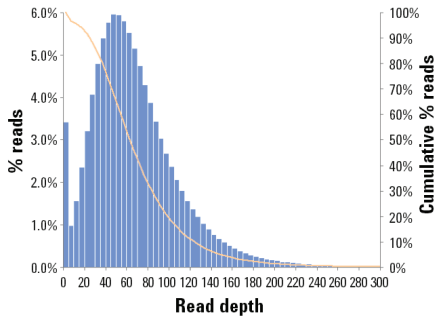

Figure 1a. Read depth of targeted regions is influenced by different enrichment efficiencies of baits and sequencing biases. Variability introduced by these factors make CNV calling from WES extremely difficult.

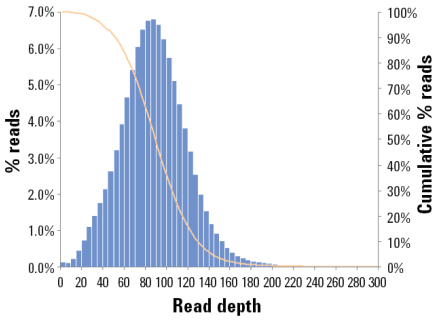

Figure 1b. The OneSeq 1Mb CNV backbone targets genomic regions with optimal GC content and mappability producing highly uniform read depth ultimately producing robust CNV calls.

Agilent Technologies

Accurately detect CNVs and chromosomal aneuploidies in addition to SNVs & indels in one assay

With OneSeq, researchers can confidently detect large chromosomal aberrations and chromosomal aneuploidies. Shown in Table 1 are CNVs and aneuploidies previously detected by Agilent CGH microarrays (aCGH). When these samples were sequenced with the OneSeq 1Mb CNV backbone plus SureSelect Human All Exon V6 for SNV and indel detection, all CNVs larger than 1Mb were detected. Sequencing libraries were prepared using 200ng of DNA with the SureSelect^{XT} Library Prep protocol. Libraries were sequenced to 100x average coverage.

Sample	Chromosome	aCGH aberration	OneSeq aberration
NA03997	12	20.7 Mb amplification	20.9 Mb amplification
NA08254	13	13.4 Mb amplification	13.2 Mb amplification
NA04592	21	Trisomy	Trisomy
NA02948	13	Trisomy	Trisomy

Table 1: CNVs and chromosomal aneuploidies detected by aCGH and OneSeq. The OneSeq design consists of the 1Mb CNV backbone plus the SureSelect Human All Exon V6 for SNV and indel calling.

Content added to the OneSeq 1Mb CNV backbone has excellent sequencing coverage

The OneSeq 1Mb CNV backbone can be combined with any SureSelect catalog exome, gene panels or custom panels for SNV and indel calling. These regions show excellent coverage even in the presence of the CNV backbone to enable accurate SNV and indel calling (Figure 2).

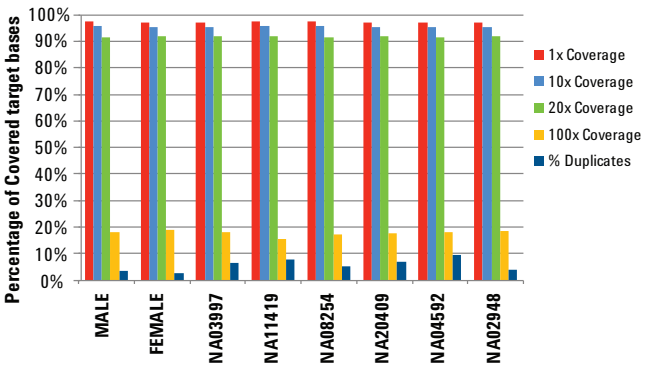

Figure 2: Depth of coverage of SureSelect Exome V6 when sequenced in combination with OneSeq 1Mb CNV backbone.

Streamlined data analysis and visualization with SureCall data analysis software

While many open source algorithms exist to call CNVs from NGS data, the time and infrastructure to implement bioinformatics pipelines can be daunting. The SureCall data analysis software can analyze OneSeq data in three simple steps. SureCall can perform read alignment followed by simultaneous detection of CNVs, LOH, SNVs, and indels, and provide annotations. SureCall also provides the ability to visualize CNVs and LOH allowing researchers to investigate the genomic context of the variants (Figure 3).

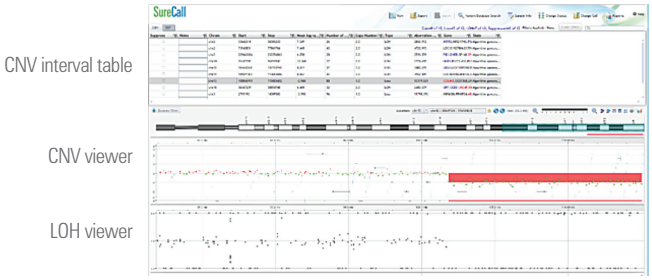

Figure 3: Data analysis and visualization using SureCall Data Analysis Software. The CNV interval table provides details about the CNV such as genomic coordinates and type of aberration. Log ratios can be viewed in the CNV viewer while the LOH viewer displays B-allele frequency.

Conclusion

OneSeq provides the ability to detect all variant types in a single cost-effective NGS assay, enabling rapid discovery of new disease-associated variants and unravelling new biological pathways involved in disease.

References

Tan R. *et al*. An evaluation of copy number variation detection tools from whole exome sequencing data. Human Mutat. 2014. 35(7):899-907

LEARN MORE AT:
www.agilent.com/genomics/OneSeq

USA and Canada
agilent_inquiries@agilent.com

Europe
info_agilent@agilent.com

Asia Pacific
inquiry_lsca@agilent.com

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