Copy Number Variation (CNV) Analysis with BeadStudio

CNV Analysis is fully supported with BeadStudio software in combination with all Illumina Infinium® DNA Analysis BeadChips.

Introduction

Illumina provides many plug-ins designed specifically for copy number variant (CNV) analysis within BeadStudio. The following list describes several plug-ins and where they can be obtained. All of these applications require BeadStudio and internet access. For the latest list of plug-ins, please visit the illumina•Connect website at http://www.illumina.com/illuminaconnect.

Table 1: CNV Analysis Options

Plug-in	Function
cnvPartition	Annotate CNV regions and copy number estimate
QuantiSNP	Provide copy number estimates with confidence scores
dChip	Provide copy number estimates and LOH scores
Homozygosity Detector	Detect extended tracts of homozygosity
LOH Score	Provide LOH scores
ChromoZone	Annotate CNV regions

cnvPartition

Summary: Developed by Illumina, this algorithm uses a recursive partitioning approach and provides copy number estimates, as well as chromosomal bookmarks.

Availability: This plug-in is currently available for BeadStudio. It can be downloaded from the BeadStudio portal or from the illumina•Connect plug-ins webpage.

Use: This plug-in is run from the Genotyping Module.

Output: Unlike ChromoZone, cnvPartition is optimized to use intensity information, and thus provides both copy number estimates and bookmarks.

Performance: 25 seconds per sample[1] (Hap550).

QuantiSNP

Summary: Developed at Oxford University, QuantiSNP has been designed and optimized for Illumina SNP genotyping and CNV data. Based on a Hidden-Markov Model[2], it provides copy number estimates and bookmarks with confidence scores. QuantiSNP is optimal for finding small-sized CNV regions.

Availability: A plug-in is required to call this algorithm in BeadStudio. This plug-in is available for download from the illumina•Connect website or the BeadStudio portal. The QuantiSNP Windows executable is also required and can be obtained by contacting Dr. Ioannis Ragoussis at (ioannisr@well.ox.ac.uk) or from the Oxford University website at http://www.well.ox.ac.uk/QuantiSNP/.

Use: The BeadStudio plug-in outputs the correct data input for QuantiSNP. The plug-in is run by selecting QuantiSNP CNV Analysis from the drop-down list of CNV Analysis algorithms in Analysis | CNV Analysis. QuantiSNP results can then be input into BeadStudio in the form of a CNV Analysis. Bookmarks can also be created within the Illumina Genome Viewer (IGV) based on the CNV Analysis.

Output: QuantiSNP provides copy number estimates with confidence scores (p-values).

Performance: Nine minutes per sample using 10 optimization steps[1] (Hap550), 40–60 minutes for Human1MDuo.

dChip

Summary: dChip was developed at Harvard (Cheng Li laboratory) and has been used on various types of microarray data[3]. It provides copy number estimates and LOH scores.

Availability: A compatible custom report plug-in is currently available for BeadStudio. This can be obtained from the illumina•Connect website, or the BeadStudio portal. The setup program will install the plug-in in the correct directory. In addition, dChip must be downloaded from http://www.hsph.harvard.edu/biostats/complab/dchip/download.htm.

Use: The custom report plug-in will provide the correct data file for input to dChip. The plug-in is run by selecting dChipGTInput Reports from the drop-down list of Custom Reports in Analysis | Reports | Report Wizard.

Output: dChip provides both copy number estimates and LOH scores.

Note: Illumina only provides a custom report plug-in that outputs BeadStudio data in a dChip compatible format. Illumina does not currently provide any further support of dChip.

Homozygosity Detector

Summary: Developed by Illumina, this algorithm searches for extended regions of homozygosity (LOH) and does not use intensity information.

Availability: This plug-in is currently available for BeadStudio.

It can be downloaded from the BeadStudio portal or from the illumina•Connect plug-ins webpage.

Use: This plug-in is run from the Genotyping Module.

Output: The Homozygosity Detector provides bookmarks.

Performance: 12 seconds per sample[1] (Hap550).

LOH Score

Summary: Developed by Illumina, this algorithm calculates values that indicate the likelihood that LOH is present in a region of interest.

Availability: This plug-in is currently available for BeadStudio. It can be downloaded from the BeadStudio portal or from the illumina•Connect plug-ins webpage.

Use: This plug-in is run through the IGV in the Genotyping Module.

Output: The algorithm provides LOH scores.

Performance: 40 seconds per sample[1] (Hap550).

ChromoZone

Summary: Developed by Illumina and first released in BeadStudio v3.0, ChromoZone is an auto-bookmarking algorithm for single samples based on the B allele frequency metric only.

Availability: ChromoZone is available as a plug-in to BeadStudio. Users can download this plug-in from a link in the BeadStudio portal, or directly from the illumina•Connect website.

Use: ChromoZone is run as a plug-in from the IGV through the BeadStudio Genotyping Module.

Output: ChromoZone provides bookmarks labeled het split and het sparse.

Performance: 22 seconds per sample1 (Hap550).

Note: This algorithm does not use intensity information, and therefore does not provide copy number estimates.

Paired-Sample Bookmarker

This algorithm is no longer be available in BeadStudio.

Copy Number Estimate

This algorithm is no longer be available in BeadStudio.

References

1. Performance measured on an Intel Pentium computer 3.4GHz processor, 2GB RAM, running Windows XP SP2.
2. Colella S, Yau C, Taylor JM, Mirza G, Butler H et al. (2007) QuantiSNP: an Objective Bayes Hidden-Markov Model to detect and accurately map copy number variation using SNP genotyping data. Nucleic Acids Res 35: 2013-2025.
3. Lin M, Wei LJ, Sellers WR, Lieberfarb M, Wong WH et al. (2004) dChipSNP: significance curve and clustering of SNP-array-based loss-of-heterozygosity data. Bioinformatics 20: 1233-1240.

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